least about 95%, at least about 97%, or at least about 99% homology to the first protein, exposing the droplet to a species such as an antibody able to bind to at least one of the first and second targets, and determining a difference in binding between the species and the first and second targets. This method can be used, for example, to identify cells that produce a particular species with specific binding capabilities (e.g., high affinity and/or high selectivity) in a physiological context. In some cases, the two (or more) targets may have substantially the same compositions or sequences, but the targets may differ in other aspects. For example, the targets may have different secondary structures, different post-translational modifications (for example, phosphorylation, acetylation, etc.), different glycosylation, different epigenetic modifications (for example, methylation), different ionization, or the like.

[0091] In another example, related targets may include chemical compounds having similar chemical structures but varying in, for example, less than 10, less than 5, less than 3, or less than 2 functional groups. In some cases, related chemical compounds have a similar chemical structure but vary in molecular weight by less than 30%, less than 20%, less than 15%, less than 10%, less than 5%, or less than 3% (relative to the lighter compound). In some embodiments, related chemical compounds have the same chemical structure but are enantiomers of one another. Other targets may include, for example, a protein, a polypeptide, a peptide, a nucleic acid, an antibody, an enzyme, a virus, a hormone, HIV or other infectious agents (e.g., viruses, bacteria, parasites, prions, etc), and toxic molecules.

[0092] It should be understood that the articles and methods described herein can be used to screen for affinity and/or selectivity of a variety of different species of interest within a fluidic droplet. In some cases, the species is introduced into the droplet during formation of the droplet (e.g., the species is a part of the discontinuous phase of the droplet). Sometimes, the species is introduced into the droplet in the absence of a cell. In other cases, the species is secreted by a cell inside the droplet. Non-limiting examples of secreted species include antibodies, hormones, signaling peptides, or the like, as discussed herein. In other embodiments, the species is produced by the cell and is released into the droplet only after rupturing the cell. Non-limiting examples of such species include proteins, polypeptides, peptides, nucleic acids, antibodies, enzymes, hormones, etc., as discussed herein. The cell may be ruptured inside the droplet, in some cases without breaking the droplet, for example. In addition, as described above, a variety of different targets may be contained in the droplet and can be assayed against the species of interest.

[0093] Accordingly, a method of screening may comprise, in one embodiment, providing a fluidic droplet contained within a liquid, the droplet containing a first target, a second target, and a cell that can produce a species able to bind with at least one of the first and second targets. The cell can be cultured within the droplet to produce a species of interest, as described herein. Those of ordinary skill in the art will be aware of techniques useful for growing cells in culture, e.g., by exposing the cells to cell culture media, oxygen, carbon dioxide, suitable temperatures, etc. The species may be exposed to the first and second targets in the droplet, e.g., by allowing the cell to secrete the species or by rupturing the cell to release the species. This can result in binding of the species to at least one of the first and/or second targets in the droplet. Additional targets and additional binding events involving the species may also occur in the droplet. Once binding occurs, a difference in binding between the species and the first and second targets can be determined. Additionally, such a method may be conducted for several droplets (e.g., arranged in an array), each droplet containing the same targets but a different cell and/or a different species. By comparing binding events (e.g., using co-localization of signaling entities) between each droplet, a species of interest with desired binding capabilities (e.g., high affinity and/or high selectivity), and, in some cases, the cell that produces the species of interest, can be identified. Furthermore, binding of the species produced by the cell to one target and not the other target may be used to identify a marker specific for a condition (e.g., a marker specific for a disease in an instance where the species binds to a diseased cell but not a healthy cell).

[0094] As another example, in one embodiment, a fluidic droplet may contain more than one entity or species in the droplet. For example, a fluidic droplet may contain a cell, a molecule produced (e.g., secreted) by the cell (e.g., an antibody), and a binding molecule (e.g., a cell surface receptor, etc.) able to bind the molecule produced by the cell. Additionally, the fluidic droplet may further contain other entities, for instance, a signaling entity, a second binding molecule that can potentially bind the secreted molecule, etc. In some embodiments, a screening assay may involve the determination of a characteristic of the secreted molecule by observing whether the secreted molecule binds to the first binding molecule and/or second binding molecule (e.g., due to the co-localization of signaling entities associated with each of the species). As described herein, in addition to molecules secreted by a cell, other types of molecules produced by a cell can be screened in this manner.

[0095] In one illustrative non-limiting example, a screening assay involves fluidic droplets containing at least three different cells. The cells may include, for example, 1) an antibody-producing cell from an animal immunized with surface proteins purified from cancer cells, 2) a labeled (e.g., cy3-labeled) cancer cell known to have surface markers of interest, and 3) a labeled (e.g., cy5-labeled) healthy cell (lacking the cell surface markers). Antibodies produced by the antibody-producing cell that are secreted within the droplets can be labeled with a third signaling entity (e.g., a fluorescent dye through interaction with an FITC-labeled anti-rabbit antibody). Co-localization of the FITC and cy3 signals brought about by binding between the secreted antibody and the cancer cell (with very low or no co-localization of the FITC and cy5 signals, meaning little or no binding between the antibody and the health cell) would indicate production of a potentially useful marker-specific antibody, while co-localization of FITC with cy3 and cy5 would indicate production of an antibody that binds both healthy and cancerous cells. This example shows that antibodies having different binding affinities/activities, as well as the cells that produce such antibodies, can be identified in physiological conditions using the articles and methods described herein.

[0096] As mentioned above, the articles and methods described herein may be used for screening of entities or species, and may include assays such as cell-based assays, non-cell-based assays, antigen capture assays, bioassays (e.g., determination of pharmacological activity of new or chemically undefined substances), competitive protein binding assays, immunoassays, microbiological assays, toxicity assays, and concentration assays, which may be, for example, quantitative or qualitative. Thus, in certain aspects of the